

CLAIMS

What is claimed is:

- 1 1. A method for bonding tissue or sealing a fluid or gas leak in tissue comprising the
2 steps of:
 - 3 (a) providing a protein, a surfactant, and a lipid in a liquid carrier;
 - 4 (b) providing a crosslinker capable of crosslinking the protein;
 - 5 (c) preparing a sealant by mixing the protein with the crosslinker under
6 conditions which permit crosslinking of the protein; and
 - 7 (d) applying the sealant of (c) to a tissue, thereby to bond the tissue or seal a
8 fluid or gas leak in the tissue.
- 1 2. A method for bonding tissue or sealing a fluid or gas leak in tissue comprising the
2 steps of:
 - 3 (a) applying to a tissue locus:
 - 4 i. a protein preparation;
 - 5 ii. at least one preparation selected from the group consisting of a
6 surfactant preparation and a lipid preparation; and
 - 7 iii. a crosslinker preparation; and
 - 8 (b) permitting the preparations to form crosslinks, thereby to bond said tissue or
9 to seal a fluid or gas leak in said tissue.
- 1 3. The method of claim 1 or 2, wherein the protein is selected from the group
2 consisting of albumin, collagen, gelatin, globulin, elastin, protamine, and histone.
- 1 4. The method of claim 3, wherein the concentration of the protein is between about
2 3% (w/w) and about 50% (w/w).
- 1 5. The method of claim 4, wherein the protein is albumin and wherein the
2 concentration of albumin is between about 20% (w/w) and about 50% (w/w).
- 1 6. The method of claim 4, wherein the protein is collagen and wherein the
2 concentration of collagen is between about 3% (w/w) and about 12% (w/w).
- 1 7. The method of claim 4, wherein the protein is a globulin and wherein the
2 concentration of the globulin is between about 15% (w/w) and about 30% (w/w).

- 1 8. The method of claim 1 or 2, wherein the concentration of surfactant is between
2 about 0.05% (w/w) and about 10% (w/w).
- 1 9. The method of claim 8, wherein the surfactant is an ionic surfactant.
- 1 10. The method of claim 9, wherein the ionic surfactant is selected from the group
2 consisting of alkanoic acids, alkylsulfonic acids, alkyl amines, perfluoroalkanoic
3 acids, and perfluoroalkylsulfonic acids.
- 1 11. The method of claim 10, wherein the ionic surfactant comprises an alkyl group
2 with a chemical formula $\text{CH}_3(\text{CH}_2)_n$, wherein n is an integer from about 6 to
3 about 18.
- 1 12. The method of claim 10, wherein the alkanoic acid is selected from the group
2 consisting of octanoic acid, dodecanoic acid and palmitic acid.
- 1 13. The method of claim 10, wherein the alkylsulfonic acid is sodium lauryl sulfate.
- 1 14. The method of claim 10, wherein the perfluoroalkanoic acid has a structure
2 selected from the group consisting of $\text{CF}_3(\text{CF}_2)_n\text{-COO-}$, and $\text{-OOC}(\text{CF}_2)_n\text{-COO-}$,
3 wherein n is an integer from one to about sixteen.
- 1 15. The method of claim 10, wherein the perfluoroalkanoic acid is perfluorooctanoic
2 acid.
- 1 16. The method of claim 1 or 2, wherein the surfactant is a nonionic surfactant.
- 1 17. The method of claim 16, wherein the nonionic surfactant is selected from the
2 group consisting of an alkyl or perfluoroalkyl- polyoxyethylene ether, a
3 polyoxyethylene ester, a polyoxyethylene sorbitan, and an alkyl aryl polyether
4 alcohol.
- 1 18. The method of claim 17, wherein the alkyl aryl polyether alcohol is tyloxapol.
- 1 19. The method of claim 1 or 2, wherein the concentration of the lipid is from about
2 0.1% (w/v) to about 10% (w/v).
- 1 20. The method of claim 1 or 2, wherein the lipid is a naturally-occurring lipid.
- 1 21. The method of claim 1 or 2, wherein the lipid is a synthetic lipid.

- 1 22. The method of claim 1 or 2, wherein the lipid is a hydrophobically-modified
2 glycerol derivative of a molecule selected from the group consisting of
3 phosphocholines, phosphatidic acid, phosphatidylethanolamine, phosphatidyl
4 inositol, glycerol, bile acids, and long chain alcohols.
- 1 23. The method of claim 22, wherein the hydrophobically-modified glycerol derivative
2 of a phosphocholine has the structure $R_1-C(O)-O-CH_2-(R_2-C(O)-O)CH_2-CH_2-$
3 $OPO_2O(CH_2)_2-N(CH_3)_3$, wherein R_1 and R_2 are chemical groups that do not react
4 with a carbodiimide.
- 1 24. The method of claim 22, wherein the hydrophobically-modified glycerol derivative
2 of a phosphatidic acid has the structure $R_1-C(O)-O-CH_2-(R_2-C(O)-O)CH_2-CH_2-$
3 OPO_2H , wherein R_1 and R_2 are chemical groups that do not react with a
4 carbodiimide.
- 1 25. The method of claim 22, wherein the hydrophobically-modified glycerol derivative
2 of a phosphatidylethanolamine has the structure $R_1-C(O)-O-CH_2-(R_2-C(O)-$
3 $O)CH_2-CH_2-OPO_2 O(CH_2)_2-NH_2$, wherein R_1 and R_2 are chemical groups that do
4 not react with a carbodiimide.
- 1 26. The method of claim 22, wherein the hydrophobically modified glycerol derivative
2 of a phosphatidyl inositol has the structure of $R_1-C(O)-O-CH_2-(R_2-C(O)-O)CH_2-$
3 $CH_2-OPO_2 O(C_6)_2H_{11}O_5$, wherein R_1 and R_2 are chemical groups that do not
4 react with a carbodiimide.
- 1 27. The method of claim 23-26, wherein the structure of R_1 is $CH_3(CH_2)_n-$, wherein
2 the structure of R_2 is $CH_3(CH_2)_m-$, wherein n is an integer from about 4 to about
3 22, and wherein m is an integer from about 4 to about 22.
- 1 28. The method of claim 23, wherein the hydrophobically-modified glycerol derivative
2 of a phosphocholine is dipalmitoylphosphatidyl choline.
- 1 29. The method of claim 22, wherein the bile acid is selected from the group
2 consisting of cholic acid, chenodeoxycholic acid, cholic acid methyl ester,
3 dehydrocholic acid, deoxycholic acid, and lithocholic acid.
- 1 30. The method of claim 22, wherein the long chain alcohol has the structure
2 $CH_3(CH_2)_n-OH$, wherein n is an integer from about six to about twenty-two.

- 1 31. The method of claim 1 or 2, wherein the crosslinker is a zero-length,
2 homobifunctional, heterobifunctional, or multifunctional crosslinker.
- 1 32. The method of claim 31, wherein the zero-length crosslinker is selected from the
2 group consisting of carbodiimides, isoxazolium salts, and carbonyldiimidazole
- 1 33. The method of claim 31, wherein the carbodiimide is 1-ethyl-3-(3-
2 dimethylaminopropyl) carbodiimide hydrochloride (EDC)
- 1 34. The method of claim 32, wherein the concentration of EDC is from about 5 to
2 about 500 mg/mL.
- 1 35. The method of claim 31, wherein the zerolength crosslinker is selected from the
2 group consisting of a carbodiimide mediated reactive ester and a carbamate.
- 1 36. The method of claim 35, wherein the reactive ester is formed from N-
2 hydroxysuccinimide or N-hydroxysulfosuccinimide.
- 1 37. The method of claim 1 or 2, wherein the surfactant is covalently attached to the
2 protein.
- 1 38. The method of claim 1 or 2, wherein the surfactant is not covalently attached to
2 the protein.
- 1 39. The method of claim 1 or 2, wherein the lipid is covalently attached to the protein.
- 1 40. The method of claim 1 or 2, wherein the lipid is not covalently attached to the
2 protein.
- 1 41. A kit for producing a protein-based tissue adhesive or sealant comprising:
2 (a) a protein preparation;
3 (b) a protein-degrading preparation; and
4 (c) a crosslinker preparation.
- 1 42. A kit for producing a protein-based tissue adhesive or sealant comprising:
2 (a) a protein preparation;
3 (b) a crosslinker preparation; and

4 (c) at least one preparation selected from the group consisting of a
5 surfactant preparation and a lipid preparation.

1 43. The kit of claim 42 further comprising at least one preparation selected from the
2 group consisting of a tissue primer preparation and a protein-degrading
3 preparation.

1 44. The kit of claim 41 or 42, wherein the protein is selected from the group
2 consisting of albumin, collagen, gelatin, globulin, elastin, protamine, and histone.

1 45. The kit of claim 44, wherein the concentration of the protein is between about 3%
2 (w/w) and about 50% (w/w).

1 46. The kit of claim 45, wherein the protein is albumin and wherein the concentration
2 of albumin is between about 25% (w/w) and about 50% (w/w)

1 47. The kit of claim 45, wherein the protein is collagen and wherein the concentration
2 of collagen is between about 3% (w/w) and about 12% (w/w).

1 48. The kit of claim 45, wherein the protein is a globulin and wherein the
2 concentration of the globulin is between about 15% (w/w) and about 30% (w/w).

1 49. The kit of claim 42, wherein the concentration of surfactant is between about
2 0.05% (w/w) and about 10% (w/w).

1 50. The kit of claim 42, wherein the surfactant is an ionic surfactant.

1 51. The kit of claim 50, wherein the ionic surfactant is selected from the group
2 consisting of alkanoic acids, alkylsulfonic acids, alkyl amines, perfluoroalkanoic
3 acids, and perfluoroalkylsulfonic acids.

1 52. The kit of claim 50, wherein the ionic surfactant comprises an alkyl group with a
2 chemical formula $\text{CH}_3(\text{CH}_2)_n$, wherein n is an integer from about 6 to about 18.

1 53. The kit of claim 51, wherein the alkanoic acid is selected from the group
2 consisting of octanoic acid, dodecanoic acid and palmitic acid.

1 54. The kit of claim 51, wherein the alkylsulfonic acid is sodium lauryl sulfate.

- 1 55. The kit of claim 51, wherein the perfluoroalkanoic acid has a structure selected
2 from the group consisting of $\text{CF}_3(\text{CF}_2)_n\text{-COO-}$, and $\text{-OOC}(\text{CF}_2)_n\text{-COO-}$, wherein
3 n is an integer from one to about sixteen.
- 1 56. The kit of claim 51, wherein the perfluoroalkanoic acid is perfluorooctanoic acid.
- 1 57. The kit of claim 42, wherein the surfactant is a nonionic surfactant.
- 1 58. The kit of claim 57, wherein the nonionic surfactant is selected from the group
2 consisting of an alkyl or perfluoroalkyl- polyoxyethylene ether, a polyoxyethylene
3 ester, a polyoxyethylene sorbitan, and an alkyl aryl polyether alcohol.
- 1 59. The kit of claim 57, wherein the alkyl aryl polyether alcohol is tyloxapol.
- 1 60. The kit of claim 42, wherein the concentration of the lipid is from about 0.1%
2 (w/v) to about 10% (w/v).
- 1 61. The kit of claim 42, wherein the lipid is a naturally-occurring lipid.
- 1 62. The kit of claim 42, wherein the lipid is a synthetic lipid.
- 1 63. The kit of claim 42, wherein the lipid is a hydrophobically-modified glycerol
2 derivative of a molecule selected from the group consisting of phosphocholines,
3 phosphatidic acid, phosphatidylethanolamine, phosphatidyl inositol, glycerol, bile
4 acids, and long chain alcohols.
- 1 64. The kit of claim 63, wherein the hydrophobically-modified glycerol derivative of a
2 phosphocholine has the structure $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-O)CH}_2\text{-CH}_2\text{-}$
3 $\text{OPO}_2\text{O(CH}_2)_2\text{-N(CH}_3)_3$, wherein R_1 and R_2 are chemical groups that do not react
4 with a carbodiimide.
- 1 65. The kit of claim 63, wherein the hydrophobically-modified glycerol derivative of a
2 phosphatidic acid has the structure $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-O)CH}_2\text{-CH}_2\text{-}$
3 OPO_2H , wherein R_1 and R_2 are chemical groups that do not react with a
4 carbodiimide.
- 1 66. The kit of claim 63, wherein the hydrophobically-modified glycerol derivative of a
2 phosphatidylethanolamine has the structure $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-O)CH}_2\text{-}$
3 $\text{CH}_2\text{-OPO}_2\text{O(CH}_2)_2\text{-NH}_2$, wherein R_1 and R_2 are chemical groups that do not
4 react with a carbodiimide.

- 1 67. The kit of claim 63, wherein the hydrophobically modified glycerol derivative of a
2 phosphatidyl inositol has the structure of $R_1-C(O)-O-CH_2-(R_2-C(O)-O)CH_2-CH_2-$
3 $OPO_2 O(C_6)_2H_{11}O_5$, wherein R_1 and R_2 are chemical groups that do not react
4 with a carbodiimide.
- 1 68. The kit of claim 64-67, wherein the structure of R_1 is $CH_3(CH_2)_n-$, wherein the
2 structure of R_2 is $CH_3(CH_2)_m-$, wherein n is an integer from about 4 to about 22,
3 and wherein m is an integer from about 4 to about 22.
- 1 69. The kit of claim 64, wherein the hydrophobically-modified glycerol derivative of a
2 phosphocholine is dipalmitoylphosphatidyl choline.
- 1 70. The kit of claim 63, wherein the bile acid is selected from the group consisting of
2 cholic acid, chenodeoxycholic acid, cholic acid methyl ester, dehydrocholic acid,
3 deoxycholic acid, and lithocholic acid.
- 1 71. The kit of claim 63, wherein the long chain alcohol has the structure $CH_3(CH_2)_n-$
2 OH , wherein n is an integer from about six to about twenty-two.
- 1 72. The kit of claim 41 or 42, wherein the crosslinker is a zero-length,
2 homobifunctional, heterobifunctional, or multifunctional crosslinker.
- 1 73. The kit of claim 72, wherein the zero-length crosslinker is selected from the
2 group consisting of carbodiimides, isoxazolium salts, and carbonyldiimidazole.
- 1 74. The kit of claim 73, wherein the carbodiimide is 1-ethyl-3-(3-
2 dimethylaminopropyl) carbodiimide hydrochloride (EDC).
- 1 75. The kit of claim 74, wherein the concentration of EDC is from about 5 to about
2 500 mg/mL.
- 1 76. The kit of claim 72, wherein the zero-length crosslinker is selected from the
2 group consisting of a carbodiimide mediated reactive ester and a carbamate.
- 1 77. The kit of claim 76, wherein the reactive ester is formed from N-
2 hydroxysuccinimide or N-hydroxysulfosuccinimide.
- 1 78. The kit of claim 42, wherein the surfactant is covalently attached to the protein.

- 1 79. The kit of claim 42, wherein the surfactant is not covalently attached to the
2 protein.
- 1 80. The kit of claim 42, wherein the lipid is covalently attached to the protein.
- 1 81. The kit of claim 42, wherein the lipid is not covalently attached to the protein.
- 1 82. A platelet-free composition for use as a tissue sealant or adhesive comprising a
2 protein solution and at least one preparation selected from the group consisting
3 of a surfactant preparation and a lipid preparation.
- 1 83. The composition of claim 82 comprising a protein solution, a surfactant
2 preparation and a lipid preparation.
- 1 84. The composition of claim 82, wherein the protein is selected from the group
2 consisting of albumin, collagen, gelatin, globulin, elastin, protamine, and histone.
- 1 85. The composition of claim 84, wherein the concentration of the protein is between
2 about 3% (w/w) and 50% (w/w).
- 1 86. The composition of claim 85, wherein the protein is albumin and wherein the
2 concentration of albumin is between about 25% (w/w) and about 50% (w/w)
- 1 87. The composition of claim 85, wherein the protein is collagen and wherein the
2 concentration of collagen is between about 3% (w/w) and about 12% (w/w).
- 1 88. The composition of claim 85, wherein the protein is a globulin and wherein the
2 concentration of the globulin is between about 15% (w/w) and about 30% (w/w).
- 1 89. The composition of claim 82, wherein the concentration of surfactant is between
2 about 0.05% (w/w) and about 10% (w/w).
- 1 90. The composition of claim 82, wherein the surfactant is an ionic surfactant.
- 1 91. The composition of claim 90, wherein the ionic surfactant is selected from the
2 group consisting of alkanoic acids, alkylsulfonic acids, alkyl amines,
3 perfluoroalkanoic acids, and perfluoroalkylsulfonic acids.
- 1 92. The composition of claim 91, wherein the ionic surfactant comprises an alkyl
2 group with a chemical formula $\text{CH}_3(\text{CH}_2)_n$, wherein n is an integer from about 6
3 to about 18.

- 1 93. The composition of claim 91, wherein the alkanoic acid is selected from the
2 group consisting of octanoic acid, dodecanoic acid and palmitic acid.
- 1 94. The composition of claim 91, wherein the alkylsulfonic acid is sodium lauryl
2 sulfate.
- 1 95. The composition of claim 91, wherein the perfluoroalkanoic acid has a structure
2 selected from the group consisting of $\text{CF}_3(\text{CF}_2)_n\text{-COO-}$, and $\text{-OOC}(\text{CF}_2)_n\text{-COO-}$,
3 wherein n is an integer from one to about sixteen.
- 1 96. The composition of claim 91, wherein the perfluoroalkanoic acid is
2 perfluorooctanoic acid.
- 1 97. The composition of claim 82, wherein the surfactant is a nonionic surfactant.
- 1 98. The composition of claim 97, wherein the nonionic surfactant is selected from the
2 group consisting of an alkyl or perfluoroalkyl- polyoxyethylene ether, a
3 polyoxyethylene ester, a polyoxyethylene sorbitan, and an alkyl aryl polyether
4 alcohol.
- 1 99. The composition of claim 98, wherein the alkyl aryl polyether alcohol is tyloxapol.
- 1 100. The composition of claim 82, wherein the concentration of the lipid is from about
2 0.1% (w/v) to about 10% (w/v).
- 1 101. The composition of claim 82, wherein the lipid is a naturally-occurring lipid.
- 1 102. The composition of claim 82, wherein the lipid is a synthetic lipid.
- 1 103. The composition of claim 82, wherein the lipid is a hydrophobically-modified
2 glycerol derivative of a molecule selected from the group consisting of
3 phosphocholines, phosphatidic acid, phosphatidylethanolamine, phosphatidyl
4 inositol, glycerol, bile acids, and long chain alcohols.
- 1 104. The composition of claim 103, wherein the hydrophobically-modified glycerol
2 derivative of a phosphocholine has the structure $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-}$
3 $\text{O)CH}_2\text{-CH}_2\text{-OPO}_2\text{O(CH}_2)_2\text{-N(CH}_3)_3$, wherein R_1 and R_2 are chemical groups that
4 do not react with a carbodiimide.
- 1 105. The composition of claim 103, wherein the hydrophobically-modified glycerol
2 derivative of a phosphatidic acid has the structure $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-}$

- 3 O)CH₂-CH₂-OPO₂H, wherein R₁ and R₂ are chemical groups that do not react
4 with a carbodiimide.
- 1 106. The composition of claim 103, wherein the hydrophobically-modified glycerol
2 derivative of a phosphatidylethanolamine has the structure R₁-C(O)-O-CH₂-(R₂-
3 C(O)-O)CH₂-CH₂-OPO₂ O(CH₂)₂-NH₂, wherein R₁ and R₂ are chemical groups
4 that do not react with a carbodiimide.
- 1 107. The composition of claim 103, wherein the hydrophobically modified glycerol
2 derivative of a phosphatidyl inositol has the structure of R₁-C(O)-O-CH₂-(R₂-
3 C(O)-O)CH₂-CH₂-OPO₂ O(C₆)₂H₁₁O₅, wherein R₁ and R₂ are chemical groups
4 that do not react with a carbodiimide.
- 1 108. The composition of claim 104-107, wherein the structure of R₁ is CH₃(CH₂)_n-,
2 wherein the structure of R₂ is CH₃(CH₂)_m-, wherein n is an integer from about 4
3 to about 22, and wherein m is an integer from about 4 to about 22.
- 1 109. The composition of claim 104, wherein the hydrophobically-modified glycerol
2 derivative of a phosphocholine is dipalmitoylphosphatidyl choline.
- 1 110. The composition of claim 103, wherein the bile acid is selected from the group
2 consisting of cholic acid, chenodeoxycholic acid, cholic acid methyl ester,
3 dehydrocholic acid, deoxycholic acid, and lithocholic acid.
- 1 111. The composition of claim 103, wherein the long chain alcohol has the structure
2 CH₃(CH₂)_n-OH, wherein n is an integer from about six to about twenty-two.
- 1 112. The composition of claim 82, wherein the surfactant is covalently attached to the
2 protein.
- 1 113. The composition of claim 82, wherein the surfactant is not covalently attached to
2 the protein.
- 1 114. The composition of claim 82, wherein the lipid is covalently attached to the
2 protein.
- 1 115. The composition of claim 82, wherein the lipid is not covalently attached to the
2 protein.

- 1 116. A method for preparing a tissue to react with a protein-based tissue sealant or
2 adhesive comprising the step of:
3 applying a primer solution at a pH of about 3.0 to 9.0 to a tissue locus.
- 1 117. The method of claim 116, wherein the primer solution comprises a buffer.
- 1 118. The method of claim 117, wherein the buffer is morpholinoethanesulfonic acid.
- 1 119. The method of claim 118, wherein the pH is about 5.
- 1 120. The method of claim 118, wherein the concentration of the buffer is about 0.5M.
- 1 121. A method for preparing a tissue to react with a protein-based tissue sealant or
2 adhesive comprising the step of:
1 applying a primer solution containing a protein crosslinker to a tissue
2 locus.
- 1 122. The method of claim 121, wherein the crosslinker is carbodiimide.
- 1 123. The method of claim 122, wherein the carbodiimide is EDC-HCl.
- 1 124. The method of claim 121, wherein the primer is a solution of carbodiimide and
2 hydroxysuccinimide.
- 1 125. The method of claim 124, wherein the carbodiimide is EDC-HCl and the
2 hydroxysuccinimide is N-hydroxysulfosuccinimide.
- 1 126. The method of claim 121, wherein the primer is a solution of a dialdehyde or a
2 polyaldehyde.
- 1 127. The method of claim 126, wherein the primer comprises glutaraldehyde or a
2 derivative thereof.
- 1 128. A method for preparing a tissue to react with a protein-based tissue sealant or
2 adhesive comprising the step of:
3 applying a primer solution comprising a molecule that promotes contact
4 between the sealant and a tissue, thereby promoting an increase in reactive
5 surface area between the sealant and the tissue.
- 1 129. The method of claim 128, wherein the molecule interacts preferentially with
2 fluorophilic surfaces.

- 1 130. The method of claim 128, wherein the molecule comprises a fluorophilic moiety.
- 1 131. The method of claim 130, wherein the fluorophilic moiety is a perfluoroalkanoic
2 acid.
- 1 132. The method of claim 131, wherein the perfluoroalkanoic acid is perfluorooctanoic
2 acid.
- 1 133. A method for increasing the degradation rate, or reducing the persistence of a
2 polymer-based tissue sealant or adhesive, comprising the step of:
3 mixing a polymer degrading agent with a sealant or adhesive before
4 applying the sealant or adhesive to a tissue.
- 1 134. A method for increasing the degradation rate, or reducing the persistence of a
2 polymer-based tissue sealant or adhesive, comprising the step of:
3 applying a polymer degrading agent to a sealant or adhesive at a tissue
4 locus, thereby increasing the degradation rate of the sealant or adhesive at the
5 tissue.
- 1 135. The method of claim 133 or 134, wherein the sealant or adhesive is selected
2 from the group consisting of protein-based, carbohydrate-based, nucleotide-
3 based, and synthetic polymer-based tissue sealants or adhesives or any
4 combination thereof.
- 1 136. The method of claim 133, wherein said tissue sealant or adhesive is protein-
2 based.
- 1 137. The method of claim 136, wherein the protein is selected from the group
2 consisting of albumin, collagen, and globulin.
- 1 138. The method of claim 133 or 134, wherein the sealant or adhesive is
2 carbohydrate-based.
- 1 139. The method of claim 138, wherein the carbohydrate is selected from the group
2 consisting of natural and synthetic poly- and oligo-saccharides.
- 1 140. The method of claim 139, wherein the carbohydrate is selected from the group
2 consisting of amylose, amylopectin, alginate, agarose, cellulose,

3 carboxymethylcellulose, carboxymethylamylose, chitin, chitosan, pectin, and
4 dextran.

1 141. The method of claim 133 or 134, wherein the degradation agent is an enzyme.

1 142. The method of claim 141, wherein the enzyme is selected from the group
2 consisting of proteases and glucanases.

1 143. The method of claim 142, wherein the protease is selected from the group
2 consisting of bromelain, trypsin, chymotrypsin, clostripain, collagenase, elastase,
3 papain, proteinase K, pepsin, and subtilisin.

1 144. The method of claim 143, wherein the protease is trypsin.

1 145. The method of claim 142, wherein the glucanase is selected from the group
2 consisting of agarases, amylases, cellulases, chitinases, dextranases,
3 hyaluranidases, lysozymes, and pectinases.

1 146. The method of claim 145, wherein the glucanase is cellulase.

1 147. The method of claim 133 or 134, wherein the degradation agent is provided in an
2 amount sufficient to promote degradation of the tissue sealant or adhesive within
3 forty days.

1 148. The method of claim 133 or 134, wherein the degradation agent is provided in an
2 inactive form, and wherein the degradation agent is activated after its application
3 to the sealant or adhesive.

1 149. The method of claim 133 or 134, wherein the tissue is selected from the group
2 consisting of connective tissue, vascular tissue, pulmonary tissue, neural tissue,
3 lymphatic tissue, dural tissue, spleen tissue, hepatic tissue, renal tissue,
4 gastrointestinal tissue, and skin.

1 150. A method for bonding tissue or sealing a fluid or gas leak in tissue comprising the
2 steps of:

3 (a) providing a solution comprising about 35% BSA, 5% DPPC, and 5%
4 Tyloxapol;

5 (b) providing a solution of about 200 mg/ml EDC;

- 6 (c) preparing a sealant by mixing the solution of step (a) with the solution of
7 step (b) in a ratio of about 10/1 (v/v); and
8 (d) applying the sealant of step (c) to a tissue, thereby to bond the tissue or
9 seal a fluid or gas leak in the tissue.

1 151. A kit for producing a protein-based tissue adhesive or sealant comprising:

- 2 (a) a solution comprising about 35% BSA;
3 (b) a crosslinker preparation comprising about 20% EDC; and
4 (c) at least one preparation selected from the group consisting of about
5 5% DPPC, about 5% Tyloxapol, and a combination thereof.

1 152. A two- component kit for producing a protein-based tissue adhesive or sealant
2 comprising:

- 3 (a) a first protein preparation; and,
4 (b) a second protein preparation mixed with a cross-linker preparation.

1 153. The kit of claim 152, wherein said first protein preparation is at an acid pH and
2 said second protein preparation is at a basic pH.

1 154. A two-component kit for producing a tissue adhesive or sealant comprising:

- 2 (a) a first sealant component at an acid pH;
3 (b) a second sealant component at a basic pH; and,
4 (c) a cross-linker preparation that is active at an intermediate pH,

5 wherein the cross-linker is activated upon mixing of (a), (b), and (c).

1 155. The kit of claim 153, wherein the pH of said first protein preparation is between
2 about 3.0 and 6.0.

1 156. The kit of claim 153, wherein the pH of said second protein preparation is
2 between about 6.5 and 10.0.

1 157. The kit of claim 152, wherein said first protein preparation and said second
2 protein preparation are selected from the group consisting of albumin, collagen,
3 gelatin, globulins, protamine, and histones.

- 1 158. The kit of claim 157, wherein said first protein preparation and said second
2 protein preparation comprise between about 3% (w/w) and about 50%(w/w) of
3 protein.
- 1 159. The kit of claim 157, wherein said first protein preparation and said second
2 protein preparation comprise albumin at between about 15% (w/w) and about
3 50%(w/w).
- 1 160. A kit for producing a protein-based tissue adhesive or sealant comprising:
2 (a) a preparation comprising a protein and a carbohydrate;
3 (b) a degradation agent; and,
4 (c) a cross-linker preparation.
- 1 161. The kit of claim 160, wherein said protein is selected from the the group
2 consisting of albumin, collagen, gelatin, globulins, protamine, and histones.
- 1 162. The kit of claim 160, wherein said protein is at a concentration of between about
2 15% and about 40%.
- 1 163. The kit of claim 160, wherein said carbohydrate is selected from the group
2 consisting of natural and synthetic poly- and oligo-saccharides.
- 1 164. The kit of claim 160, wherein said carbohydrate is selected from the group
2 consisting of of amylose, amylopectin, alginate, agarose, cellulose,
3 carboxymethylcellulose, carboxymethylamylose, chitin, chitosan, pectin, and
4 dextran.
- 1 165. The kit of claim 160, wherein said carbohydrate is at a concentration of between
2 about about 0.1% (w/w) and about 10% (w/w).
- 1 166. The kit of claim 160, wherein said degradation agent is selected from the group
2 consisting of proteases and glucanases.
- 1 167. The kit of claim 166, wherein said glucanases is an alginase.